Effects of L-Deprenyl on Human Growth Hormone Secretion

M. Koulu and R. Lammintausta

Department of Pharmacology, Institute of Biomedicine, University of Turku, Turku, Finland

With 4 Figures

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Summary

The effects of L-deprenyl on L-dopa-, apomorphine- and L-tryptophan-induced growth hormone (GH) secretion were studied in thirteen healthy male volunteers.

An acute 10 mg dose of L-deprenyl did not stimulate the basal GH secretion. Short-term L-deprenyl premedication significantly enhanced the L-dopa-stimulated GH release. In contrast, L-deprenyl premedication did not change the GH response to apomorphine or L-tryptophan.

Potentiation of L-dopa-induced GH release by L-deprenyl indicates an increased availability of dopamine at the receptor level without a direct agonistic effect by the drug. Furthermore, L-deprenyl does not change the function of postsynaptic dopamine receptors involved in human GH release.

Introduction

L-deprenyl is a selective inhibitor of monoamine oxidase (MAO) type B (Knoll and Magyar, 1972), which is proposed to be the main form of MAO for the oxidative deamination of dopamine in human brain (Glover et al., 1977). Additionally, L-deprenyl may intensify the synaptic action of dopamine by inhibiting its re-uptake into the presynaptic neuron (Knoll, 1978). In the clinical use L-deprenyl potentiates the anti-akinetic effects of L-dopa in parkinsonian patients and especially relieves the “on-off” phenomenon (Birkmayer et al., 1975, 1977; Lees et al., 1977; Rinne et al., 1978).
Dopamine is generally believed to act as a stimulatory neurotransmitter in the neuroendocrine regulation of human growth hormone (GH) secretion: L-dopa (Boyd et al., 1970; Eddy et al., 1971; Kansal et al., 1972) and the direct dopamine receptor agonists, including apomorphine and bromocriptine, are capable of stimulating GH secretion in healthy subjects (Lal et al., 1972; Camanni et al., 1975). The potentiating effects of L-deprenyl on the L-dopa treatment of Parkinson's disease led us to investigate whether L-deprenyl modifies basal or dopamine-controlled human GH secretion. To have more detailed information on dopamine-stimulated GH secretion we have used apomorphine as a direct dopamine receptor agonist and L-dopa as an agonist acting through the uptake and release mechanisms of the presynaptic neuron. Because it has been reported that L-deprenyl potentiates the antidepressant response to 5-hydroxytryptophan in affectively ill patients (Mendlewicz and Youdim, 1978; Youdim, 1980), in higher doses than used in Parkinson's disease, the effect of L-deprenyl premedication on the L-tryptophan-induced GH secretion was also studied.

Subjects and Methods

Thirteen healthy male volunteers participated in the study. Their ages ranged between 19 and 27 years (mean 21.8 years). The mean height was 179 ± 1 cm (mean ± S.E.M.) and the mean weight was 71 ± 2 kg. To test the possible effect of L-deprenyl on basal GH secretion the volunteers (n=9) were given, in random order as a double-blind study, either placebo or 10 mg of L-deprenyl per os (supplied by Farmos Group Ltd., Turku, Finland). Blood samples for GH analysis were taken by venepuncture before and at 30, 60, 90, 120, 150, 180 and 210 min after medication. The effects of L-deprenyl on apomorphine, L-dopa and L-tryptophan stimulation tests were studied after placebo and L-deprenyl premedication: 5 mg of L-deprenyl per os was given 24 hours before the tests and an additional 10 mg of L-deprenyl 10 hours before the tests. In the apomorphine test the volunteers (n = 6) were given 0.35 mg apomorphine hydrochloride subcutaneously, and the blood samples were taken before and at 30, 45, 60, 90 and 120 min. In the L-dopa test seven volunteers were given 200 mg L-dopa with 50 mg benserazide per os (Madopar®, Hoffmann-La Roche, Basel, Switzerland). The blood samples were taken before and at 30, 60, 90, 120 and 150 min after the L-dopa. In the L-tryptophan test the volunteers (n = 8) were given 80 mg/kg L-tryptophan (supplied by The Pharmaceutical Plant Leiras, Turku, Finland) in a capsular form. The blood samples were collected as in the L-dopa test. All the tests were carried out after an overnight fast by starting at 8.00 a.m. Between the placebo and L-deprenyl trials there was at least one week's interval. If the same